Claim 61 A protein having a molecular weight of 55-65 kD, said protein occurring naturally in a plant and having carbohydrate oxidizing activity.

Claim 62 A protein according to claim 61, wherein the protein is a hexose oxidase.

Claim 63 A protein according to claim 62, wherein the protein occurs naturally in sunflower or lettuce.

REMARKS

The Official Action of April 26, 2000 has been carefully considered and reconsideration of the application as amended is respectfully requested.

Claims 1-6, 11, 39-41 and 45 have been cancelled and rewritten as new claims 51-63. The claims have been rewritten to render them more definite and to remove the bases for the rejections under 35 USC 112, first and second paragraphs. New independent claims 51, 56, 57, 58, 59, 60 and 61 correspond to original claims 1, 3, 4, 5, 6, 11 and 39 respectively. The new claims contain the recitations in the claims which they replace and draw support from the specification in the same manner. The recitations in the claims pertaining to the identity of the muteins and their respective proteins draw support from the specification as filed at page 11, lines 5 - 8. With specific respect to the recitation in claim 54, it is noted that "one or more amino acids" (specification at page 11, line 7) contemplates only one as well as a plurality of amino acids.

Applicants hereby affirm their election of the claims of Group I and the species of sunflower. All of the newly added claims are directed to the invention of Group I and read on the elected species.

Certain claims had been rejected under 35 USC 112, second paragraph because they recited a broad range or limitation together with a narrow range or limitation in the same claim. The claims as amended are free of this informality and are otherwise believed to be sufficiently definite to satisfy the dictates of 35 USC 112, second paragraph.

Claims 1-6, 11, 39-41 and 45 were rejected under the written description requirement of 35 USC 112, first paragraph. Applicants respectfully traverse this rejection.

With respect to the claims reciting the specific SEQ ID NOs (formerly claims 1, 2, 4 - 6 and 11; now claims 51 - 55 and 57 - 60), the Examiner maintained that the description in the specification of the recited SEQ ID NOs ("species") allegedly does not show possession of a genus including the sequences and the recited muteins and sequence parts. However, Applicants respectfully note that adequate support under the written description requirement for claims to a genus does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. See, e.g., Revised Interim Guidelines for Examination of Patent Applications Under 35 USC 112, Paragraph 1 "Written Description" Requirement ("Revised Description Guidelines"), 64 Fed. Reg. 71427. For a claim to a genus, the written description requirement may be satisfied by sufficient description of a representative number of species. Id.

In the present case, the subject claims have been amended to limit the recited muteins to those that have sufficient identity to the amino acid sequences of the described species such that they retain the antifungal activity thereof. As so limited, the genus of proteins that are muteins of the recited SEQ ID NOs does not have substantial variation since all of the muteins must possess a substantial identity to the recited SEQ ID NOs and must possess the recited antifungal activity. The species disclosed are thus representative of the claimed genus because all members of the genus must have the recited identity and activity. Under these circumstances, one of skill in the art would conclude that, as of the application filing date, Applicants were in possession of the necessary common attributes possessed by the members of the genus such that the disclosure meets the written description requirements of 35 USC 112, first paragraph. See Example 14 of the Examiner Training Materials issued in connection with the Revised Description Guidelines (copy submitted herewith).

With respect to claims 56 and 61, the Examiner has contended that these claims are directed to all possible proteins having the recited activity, but this respectfully ignores the recitations requiring that the recited proteins be a plant protein or obtainable from a plant. Applicants have now amended the applicable claims to make this more definite by reciting that the claimed proteins, in addition to having the recited carbohydrate oxidase and/or antifungal activity and (with respect to claim 39) the recited molecular weight, also occur naturally in a plant.

Applicants respectfully note that the USPTO has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the original disclosure a description of the invention defined by the claims ("see Revised Description

Guidelines"). It is respectfully submitted that the Examiner cannot meet the initial PTO burden merely by contending that the claims *may* read on other proteins occurring naturally in a plant that have the recited activity and molecular weight in the absence of evidence or reasoning to show that a) such other proteins exist and b) there is substantial variation between such other proteins and those described in the specification (see Revised Description Guidelines). The Examiner has not presented evidence or reasoning in this respect. Patent application WO95/14784 was cited in the International Search Report and discloses a glucose oxidase having antifungal properties. However, the glucose oxidase disclosed in this document was not obtainable from, or naturally occurring in, a plant. Indeed, prior to the Applicants' invention, isolated proteins having carbohydrate oxidase and antifungal activity that occurred naturally in a plant were unknown.

In the absence of evidence or reasoning of the type discussed, it is respectfully submitted that the USPTO has not set forth a *prima facie* rejection of the subject claims under the written description requirement. This is *a fortiori* the case for claims 39 - 41 which are directed to a naturally occurring plant protein having the recited molecular weight and the recited activity. Plant proteins falling within such a genus would be expected to have structural features common to the members of the genus, which features constitute a substantial portion of the genus. Under these circumstances, the specification would be sufficient to satisfy the written description requirement (see *University of California v. Eli Lilly and Co.*, 43 USPQ 1398, 1406 (Fed. Cir. 1997)).

The Examiner also rejected claims 1 - 6, 11, 39 - 41 and 45 under 35 USC 112, first paragraph, for alleged lack of enablement. Applicants respectfully traverse this rejection.

As discussed above, the applicable claims have been limited to muteins that have a substantial identity with the specific sequences described in the specification. In other words, changes to the recited SEQ ID NOs must be minimal and the resultant muteins must retain the antifungal activity of the recited sequences. Such muteins can readily be made by protein engineering techniques that were well known to those of skill in the art at the time of the invention, including for example changing the open reading frames that are described in the specification as encoding the SEQ ID NOs so as to produce the recited muteins. Significantly, the specification describes and exemplifies methods routinely to test proteins (including muteins) to ascertain whether they have the recited antifungal activity (see specification at, e.g., page 10, lines 5- 17 and Examples 3, 8, 9 and 16). Any mutein of the recited sequences can be routinely tested according to methods described in the specification. Under these circumstances, the experimentation, if any, needed to practice the invention as claimed cannot be considered to be "undue".

With respect to the claims reciting that the recited proteins occur naturally in plants, it is similarly respectfully submitted that any experimentation required to isolate such proteins would be routine (not "undue"). This is true in view, for example, of the provision in the detailed description in the specification, including the Examples, of methods for such isolation (see, for example, page 10, lines 1-29 and the Examples). Under these circumstances, the specification is believed to enable those of skill in the art to practice the invention defined in each of the claims as amended without undue experimentation.

The Examiner has rejected the claims under 35 USC 102 as allegedly being anticipated by one or more of Stougaard et al, Hu et al and Woloshuk et al. Applicants respectfully traverse

these rejections.

In applying the rejections, the Examiner has not provided any explanation of where in the cited references, if at all, there appears a disclosure of the specific sequences covered by the recited SEQ ID NOs. Accordingly, it is believed that the rejections of the claims reciting such sequences are based upon an expansive reading of the term "muteins" as that term appeared in the claims as filed. As discussed above, the applicable claims have now been limited such that they cover only muteins having a substantial identity with the recited SEQ ID NOs and having the claimed antifungal activity. In the absence of a teaching in the references of the claimed sequences, it is respectfully submitted that the rejection should be withdrawn. If the Examiner considers any of the references to teach the claimed sequences, he is respectfully requested to point to the applicable portion of any such reference, as would be required to set forth a *prima facie* case of alleged anticipation.

With respect to claims 51 and 61, the claims have been amended to recite that the claimed proteins occur naturally in a plant. None of the cited references shows proteins that meet this recitation. For example, Stougaard et al teach "a method of producing recombinantly a hexose oxidase from a number of different marine *algal* species for use as an antimicrobial agent" (emphasis added). There is nothing in the cited reference to show or suggest proteins from a plant species as claimed or that the proteins of the described algal species occur naturally in a plant.

In view of the above, all rejections and objections of record are believed to have been successfully traversed and the application is believed to be in allowable form. An early notice

of allowability is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

CLIFFORD J. MASS
LADAS & PARRY
26 WEST 61ST STREET
NEW YORK, NY 10023
REG. NO. 30,086 (212) 708-1890

cjm
d:\docs\12121amd.sep

Example 14: Product by Function

Specification: The specification exemplifies a protein isolated from liver that catalyzes the reaction of A $\longrightarrow$ B. The isolated protein was sequenced and was determined to have the sequence as set forth in SEQ ID NO: 3. The specification also contemplates but does not exemplify variants of the protein wherein the variant can have any or all of the following: substitutions, deletions, insertions and additions. The specification indicates that procedures for making proteins with substitutions, deletions, insertions and additions is routine in the art and provides an assay for detecting the catalytic activity of the protein.

Claim:

A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A $\longrightarrow$ B.

Analysis:

A review of the full content of the specification indicates that a protein having SEQ ID NO: 3 or variants having 95% identity to SEQ ID NO: 3 and having catalytic activity are essential to the operation of the claimed invention. The procedures for making variants of SEQ ID NO: 3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO: 3 which have 95% identity to SEQ ID NO: 3 and retain its activity are conventional in the art.

A review of the claim indicates that variants of SEQ ID NO: 3 include but are not limited to those variants of SEQ ID NO: 3 with substitutions, deletions, insertions and additions; but all variants must possess the specified catalytic activity and must have at least 95% identity to the SEQ ID NO: 3. Additionally, the claim is drawn to a protein which **comprises** SEQ ID NO: 3 or a variant thereof that has 95% identity to SEQ ID NO: 3. In other words, the protein claimed may be larger than SEQ ID NO: 3 or its variant with 95% identity to SEQ ID NO: 3. It should be noted that "having" is open language, equivalent to "comprising".

The claim has two different generic embodiments, the first being a protein which comprises SEQ ID NO: 3 and the second being variants of SEQ ID NO: 3. There is a single species disclosed, that species being SEQ ID NO: 3.

A search of the prior art indicates that SEQ ID NO: 3 is novel and unobvious.

There is actual reduction to practice of the single disclosed species. The specification indicates that the genus of proteins that must be variants of SEQ ID NO: 3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO: 3. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity. One of skill in the art would conclude that

applicant was in possession of the necessary common attributes possessed by the members of the genus.

Conclusion: The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.